Survival of Blood Platelets Labeled with Chromium^{51}

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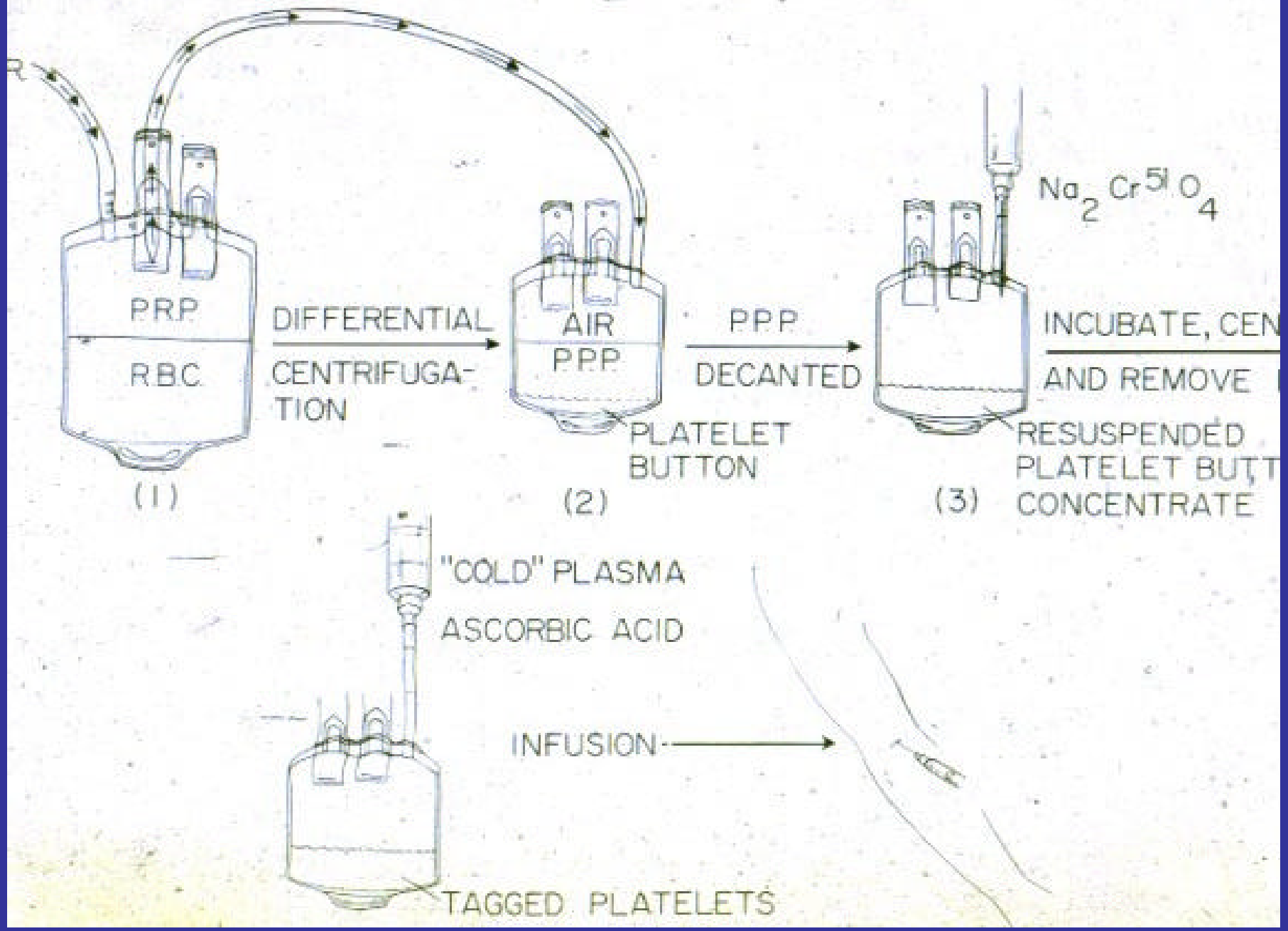
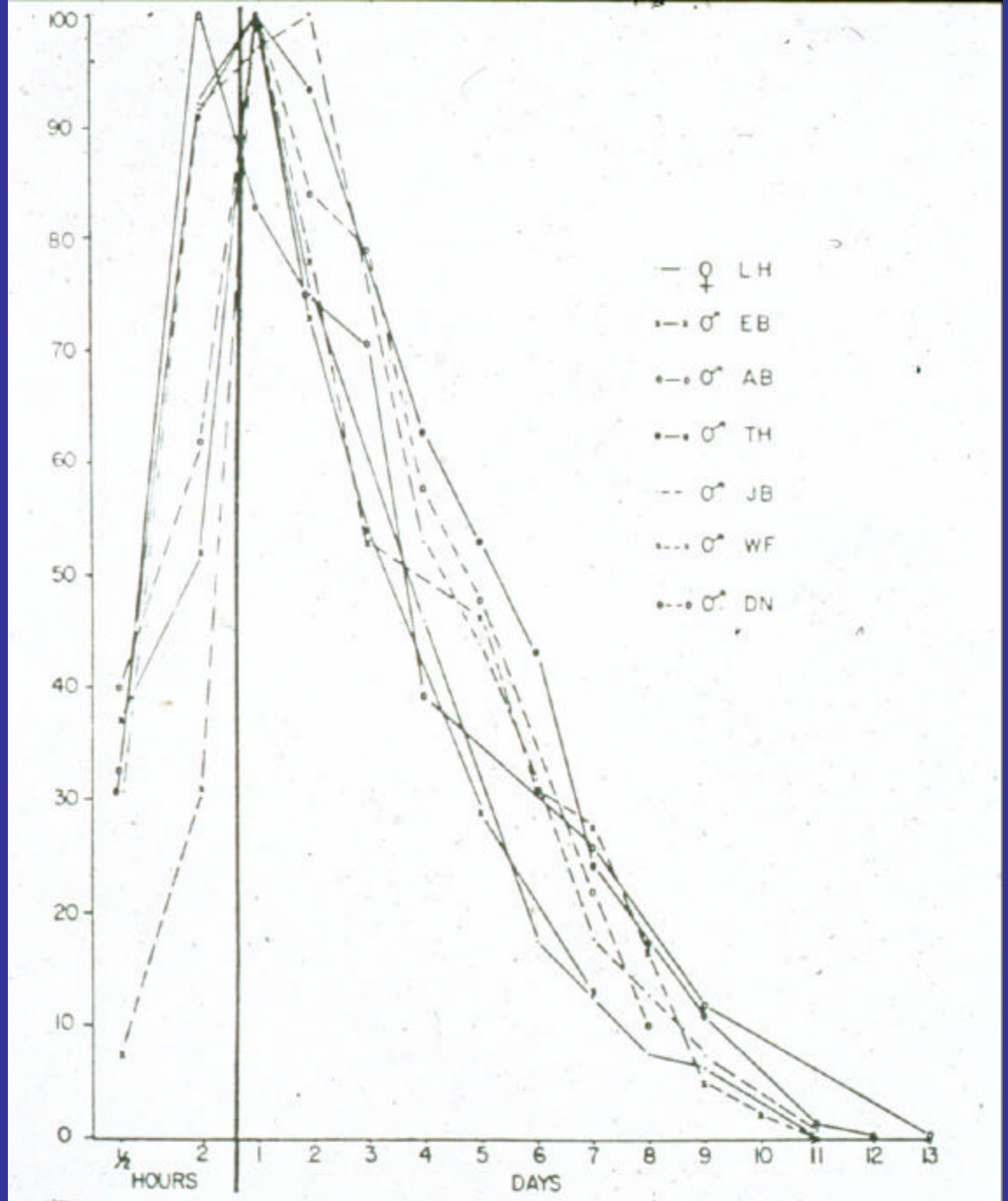
J Clin Invest 37;1257, 1958

1. Anticoagulant. Plasma preparations prepared with acid citrate dextrose (ACD) solution (National Institutes of Health formula) have numerous microscopic aggregations of platelets that do not resuspend after centrifugation and labeling with Cr^{51}. Earlier studies have demonstrated that platelets are discrete and not clumped when NA^2EDTA was used as the anticoagulant.

Aas, Gardner J Clin Invest 37:1257, 1958


PRP
RBC
(1)
DIFFERENTIAL
CENTRIFUGATION
AIR
PPP
PLATELET
BUTTON
(2)
PPP
DECANTED
$Na_2Cr^{51}O_4$
INCUBATE, CEN
AND REMOVE
RESUSPENDED
PLATELET BUTT
CONCENTRATE
(3)
"COLD" PLASMA
ASCORBIC ACID
INFUSION
TAGGED PLATELETS



Aas, Gardner J Clin Invest 37:1258, 1958

Aster's Solution

0.085 M Na_3 Citrate

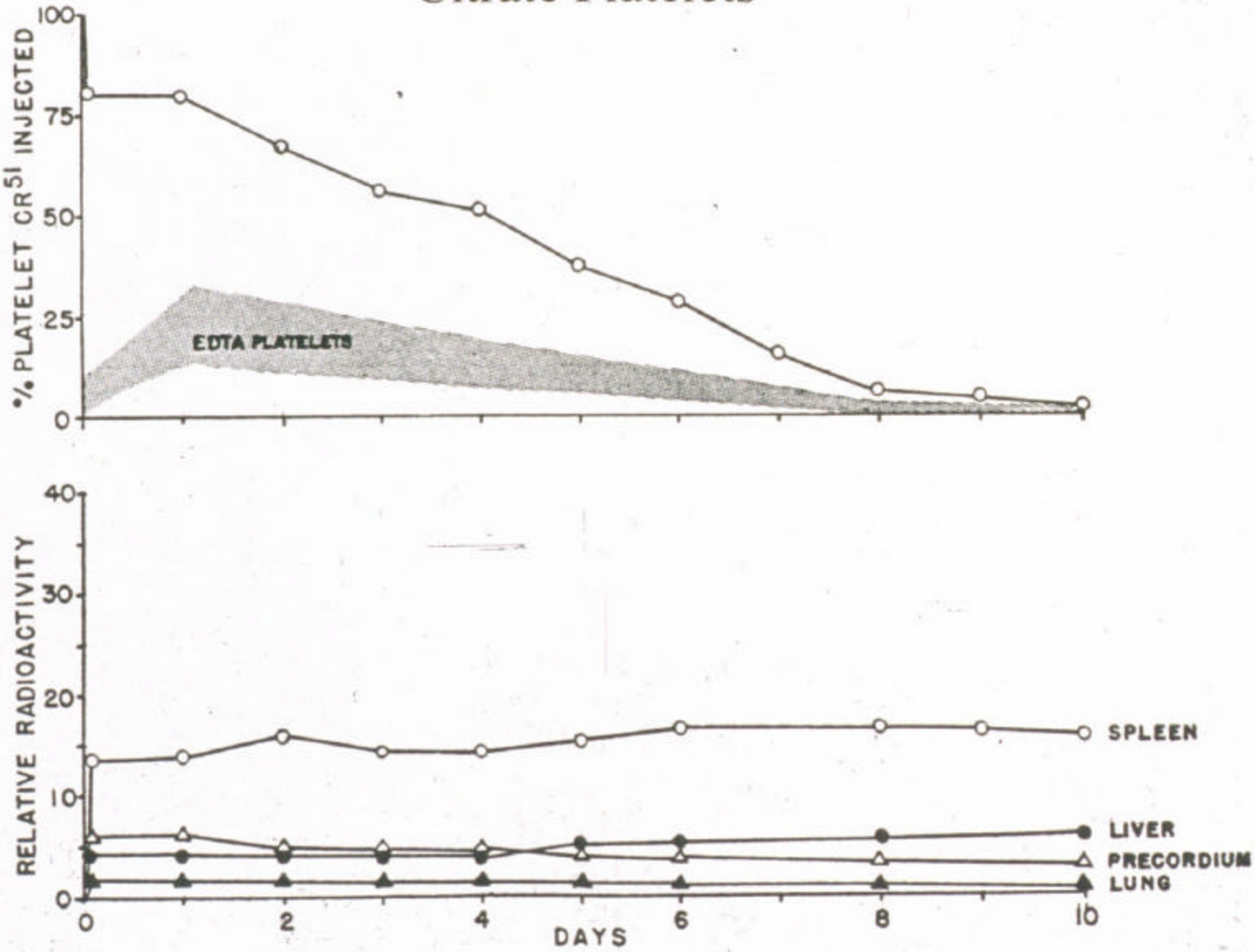
0.065 M Citric Acid

2% Dextrose

Blood pH, 6.5

Citrate, 0.022M
(Increased 50%)

No Sequestration
Citrate Platelets

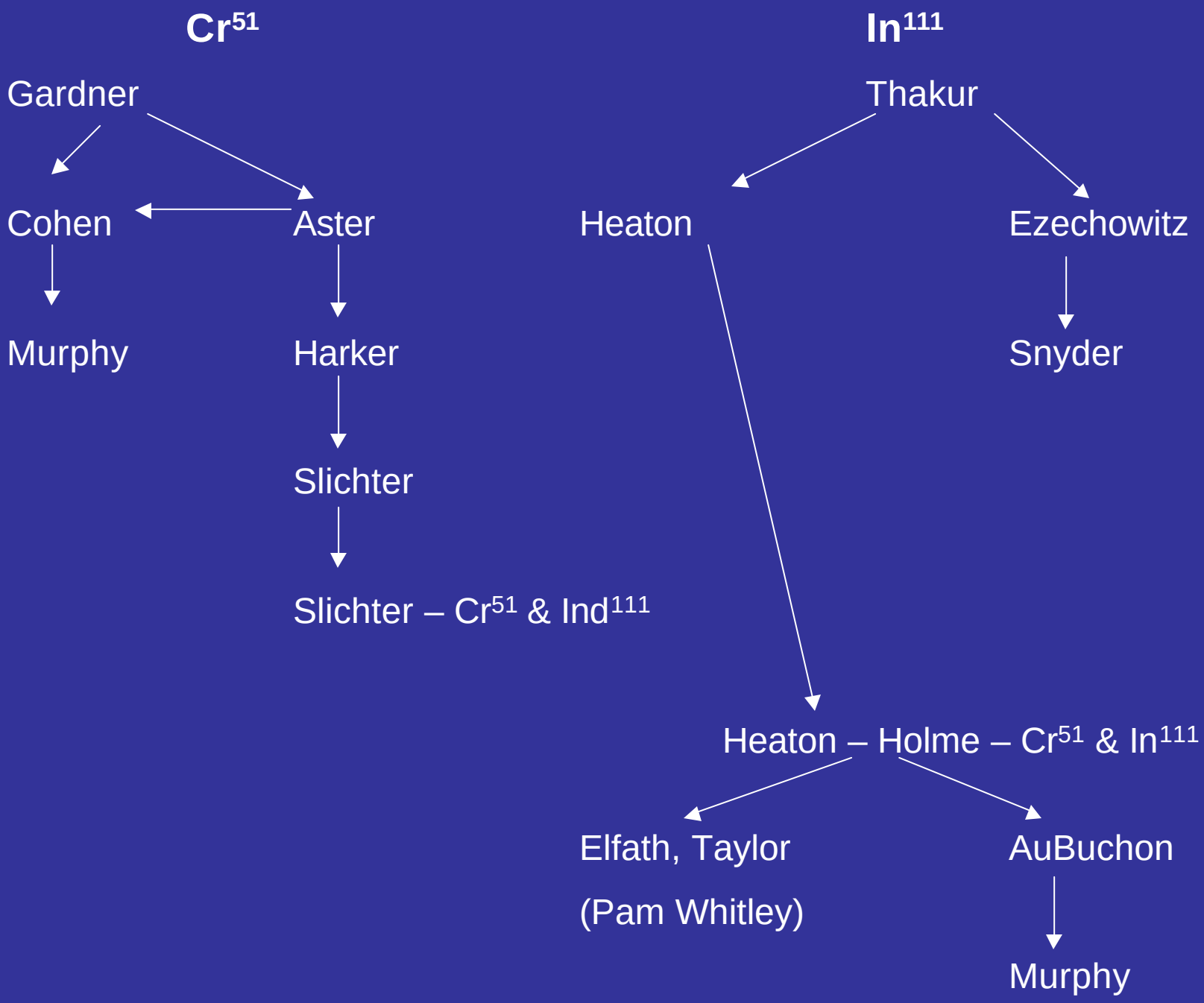


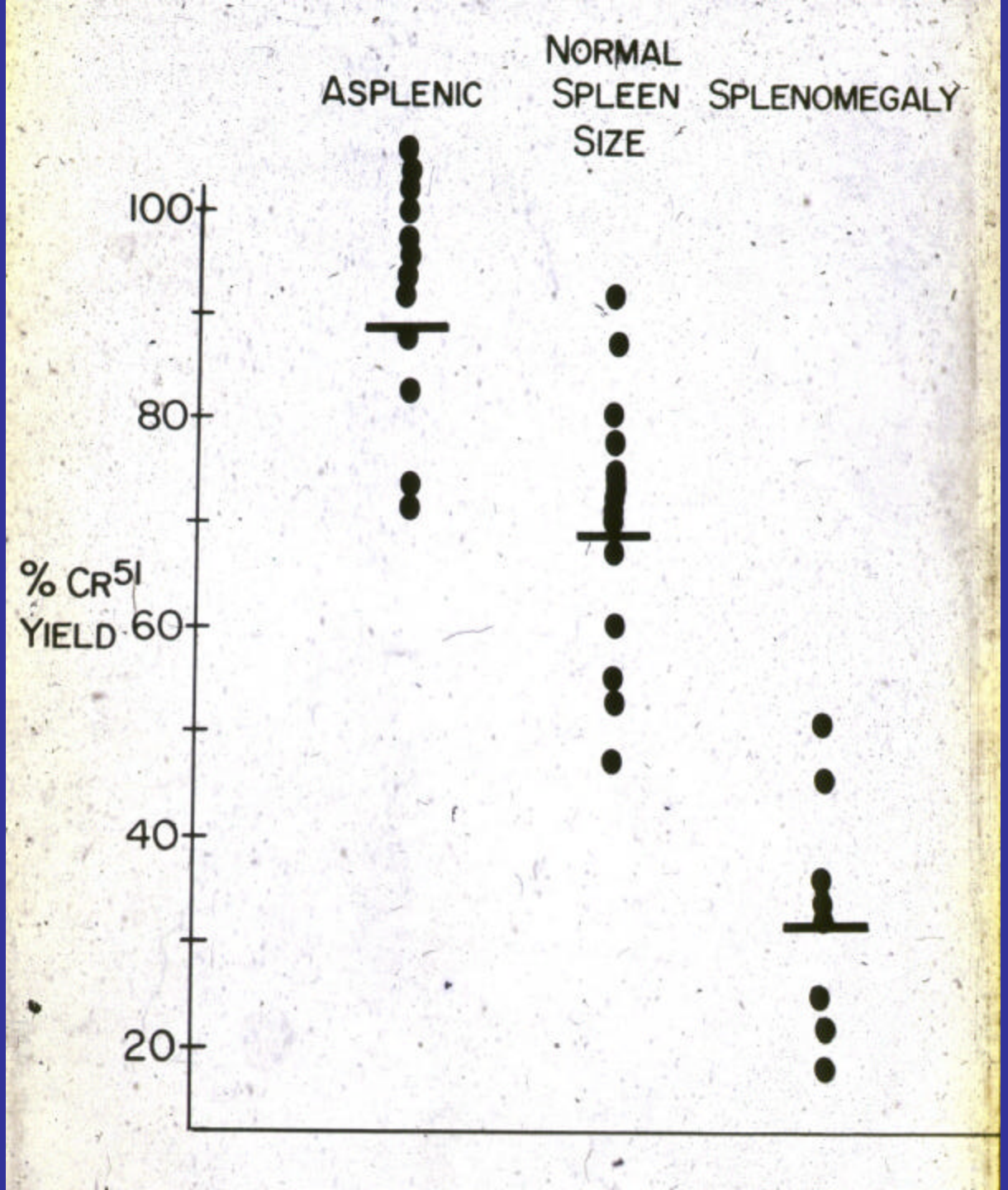
Aster, Jandl JCI 43:843, 1964

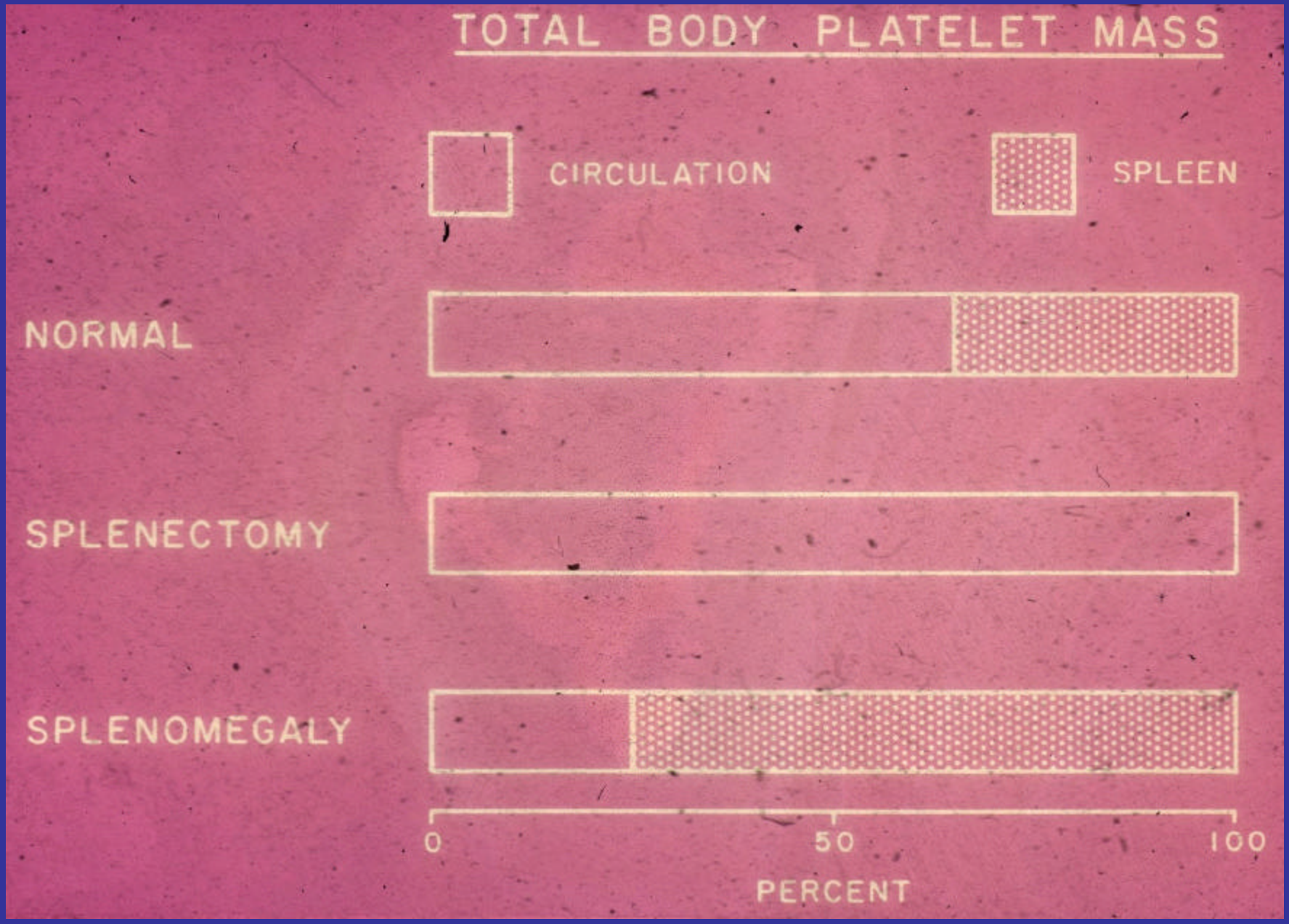
Platelet Preservation III
Comparison of Radioactivity Yields of Platelet Concentrates Derived From Blood Anticoagulated with EDTA and ACD

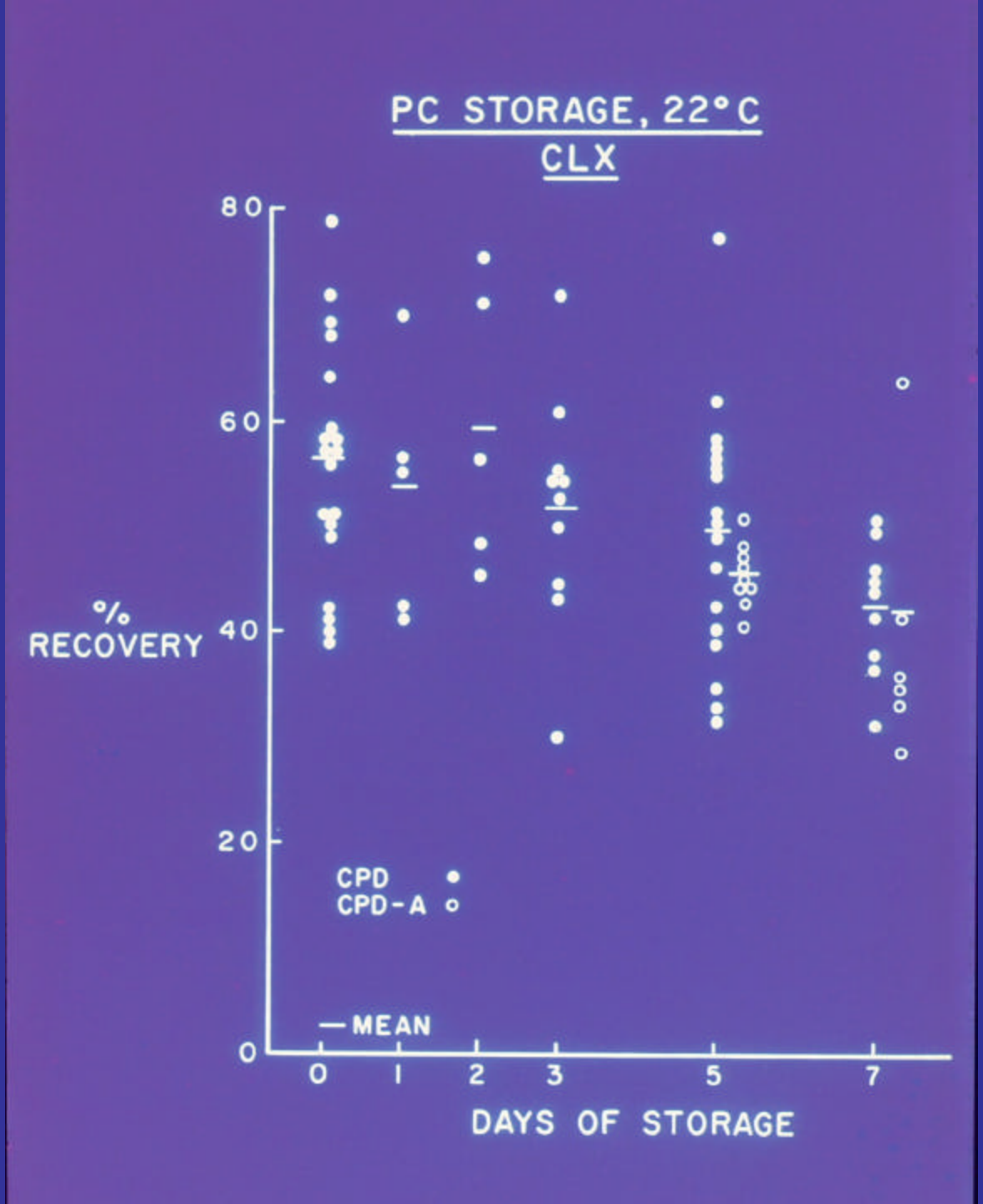
Phil Cohen, Mark H. Cooley, Frank H. Gardner

New England Journal of Medicine
273:845-850, 1965


Cr51
Gardner
Cohen
Aster
Murphy
Harker
Slichter
Slichter – Cr51 & Ind111
In111
Thakur
Heaton
Ezechowitz
Snyder
Heaton – Holme – Cr51 & In111
Elfath, Taylor
(Pam Whitley)
AuBuchon
Murphy

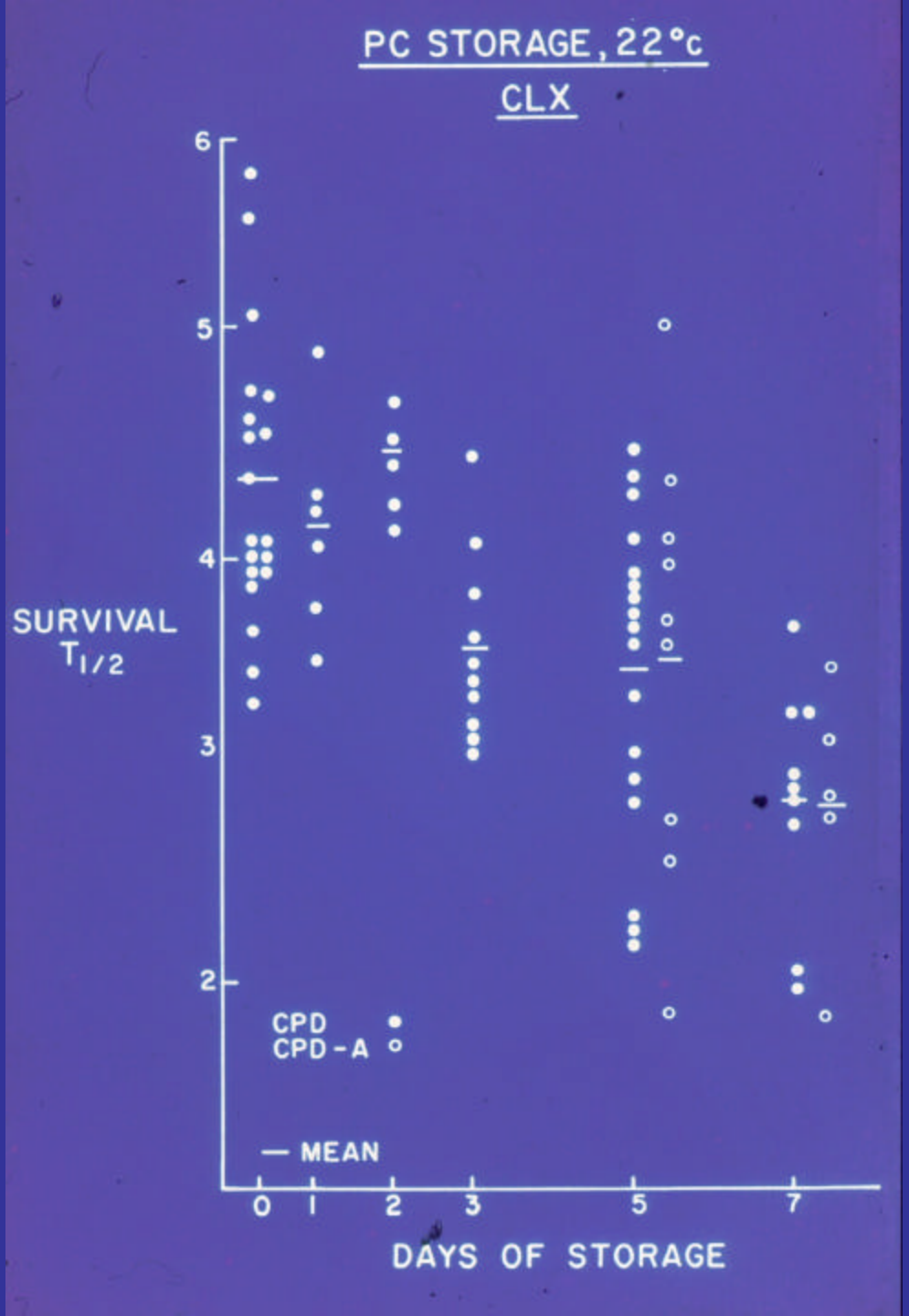

ASPLENIC
NORMAL SPLEEN SIZE
SPLENOMEGALY
100
80
60
40
20
% CR51 YIELD

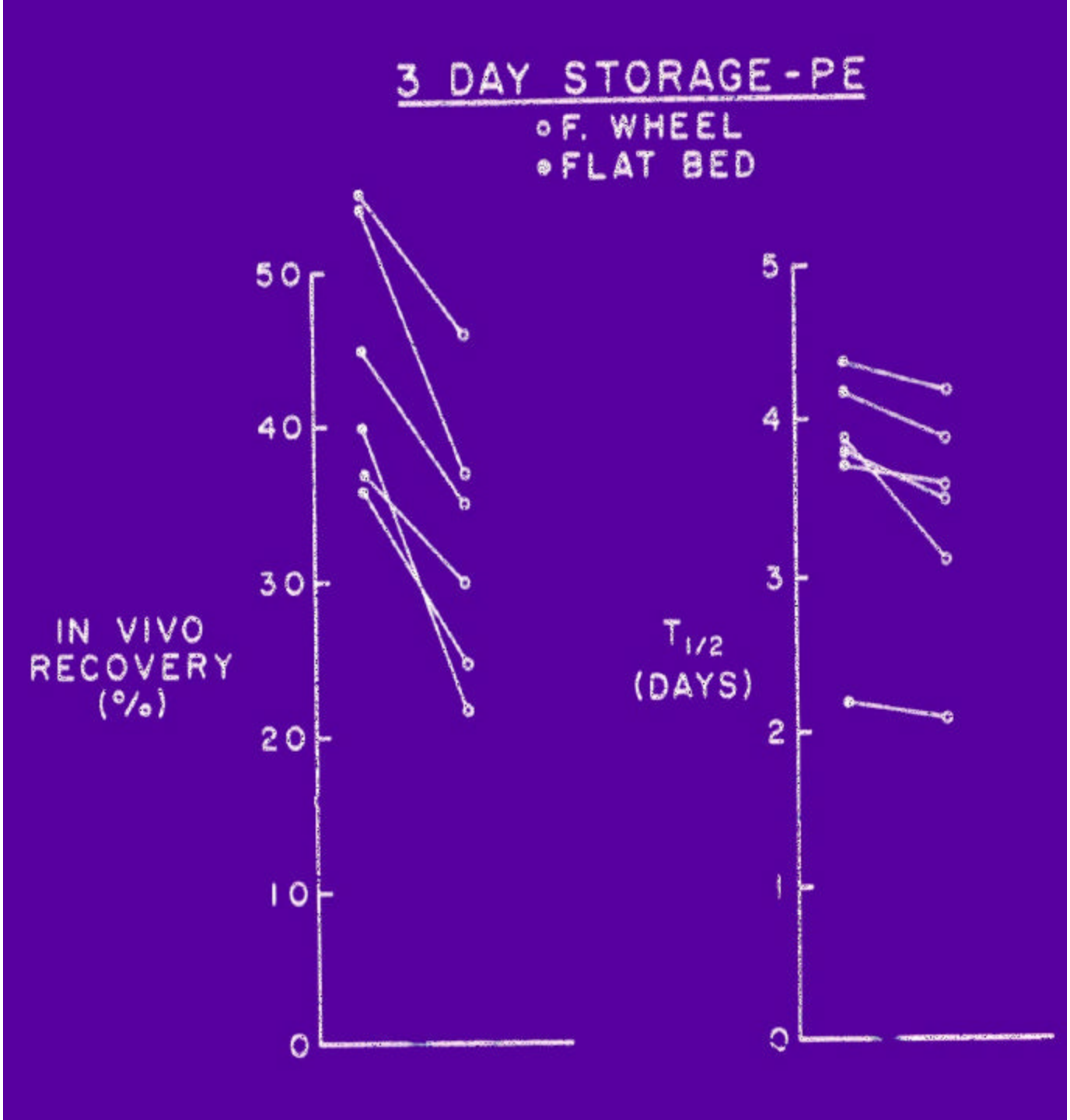

TOTAL BODY PLATELET MASS
CIRCULATION
SPLEEN
NORMAL
SPLENECTOMY
SPLENOMEGALY
0
50
100
PERCENT

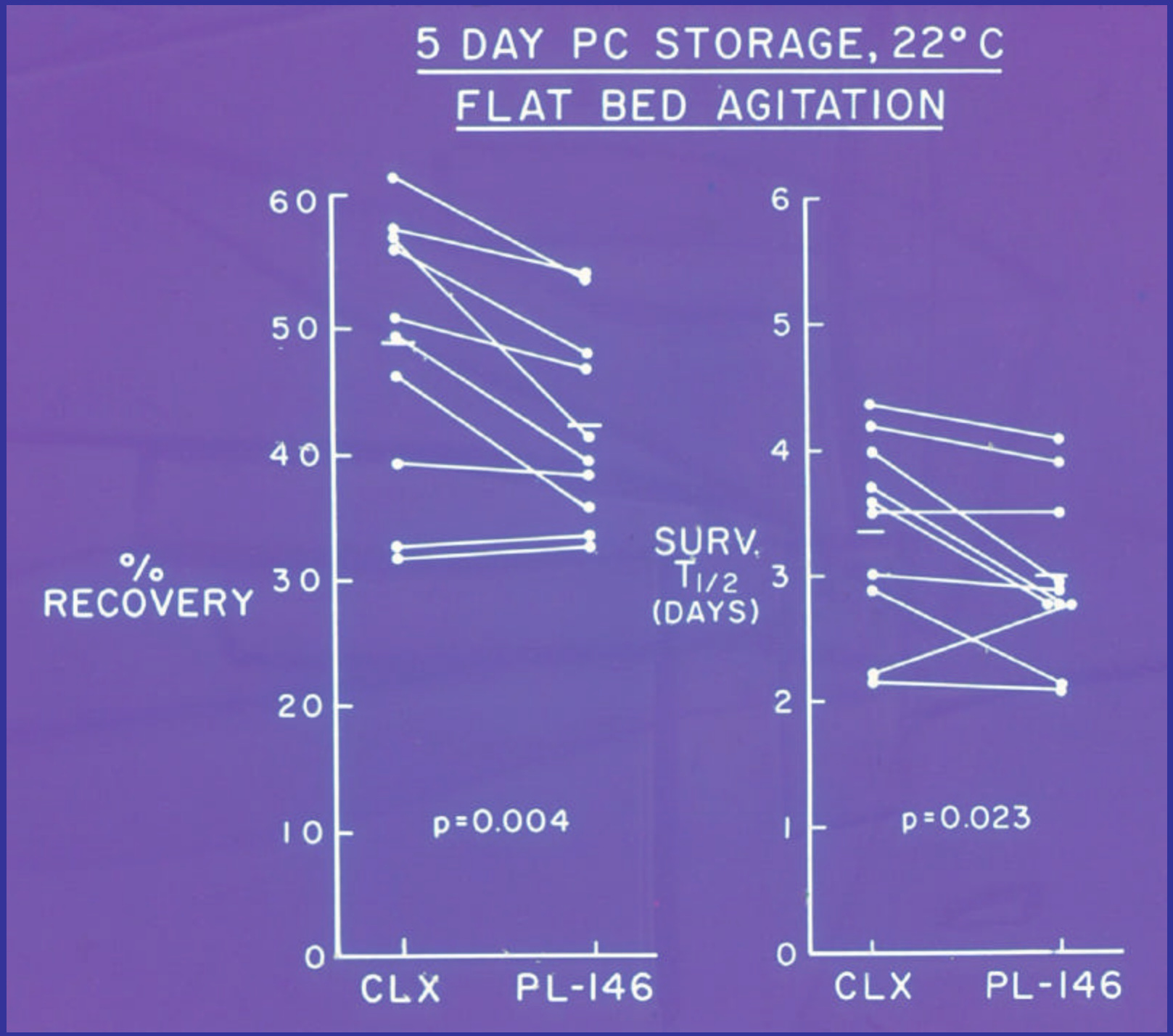

PC STORAGE, 22°C
CLX
80
60
40
20
0
% RECOVERY
CPD
CPD-A
— MEAN
0
1
2
3
5
7
DAYS OF STORAGE

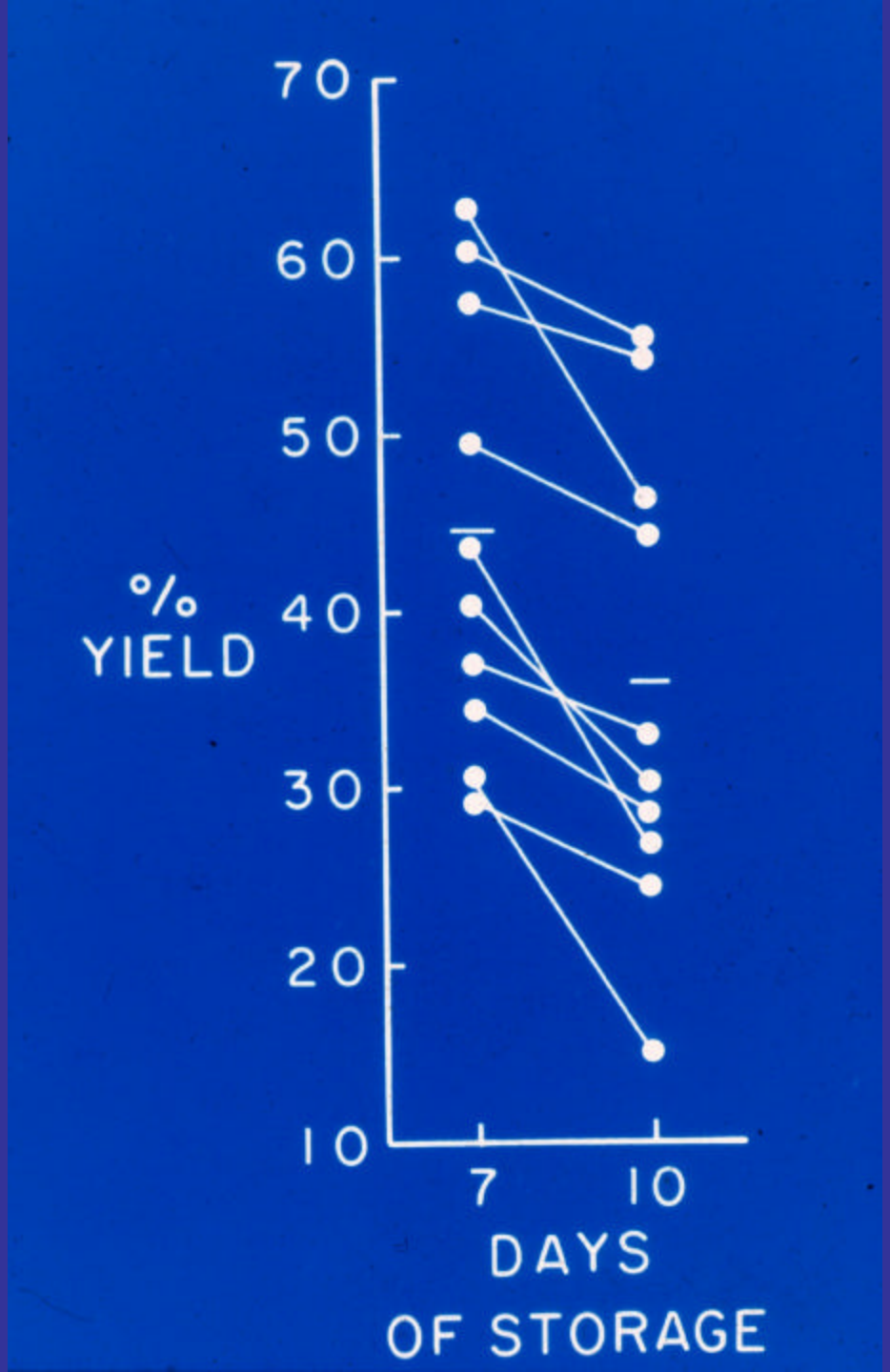
Normal Population
Recoveries Fresh Platelets-Variable

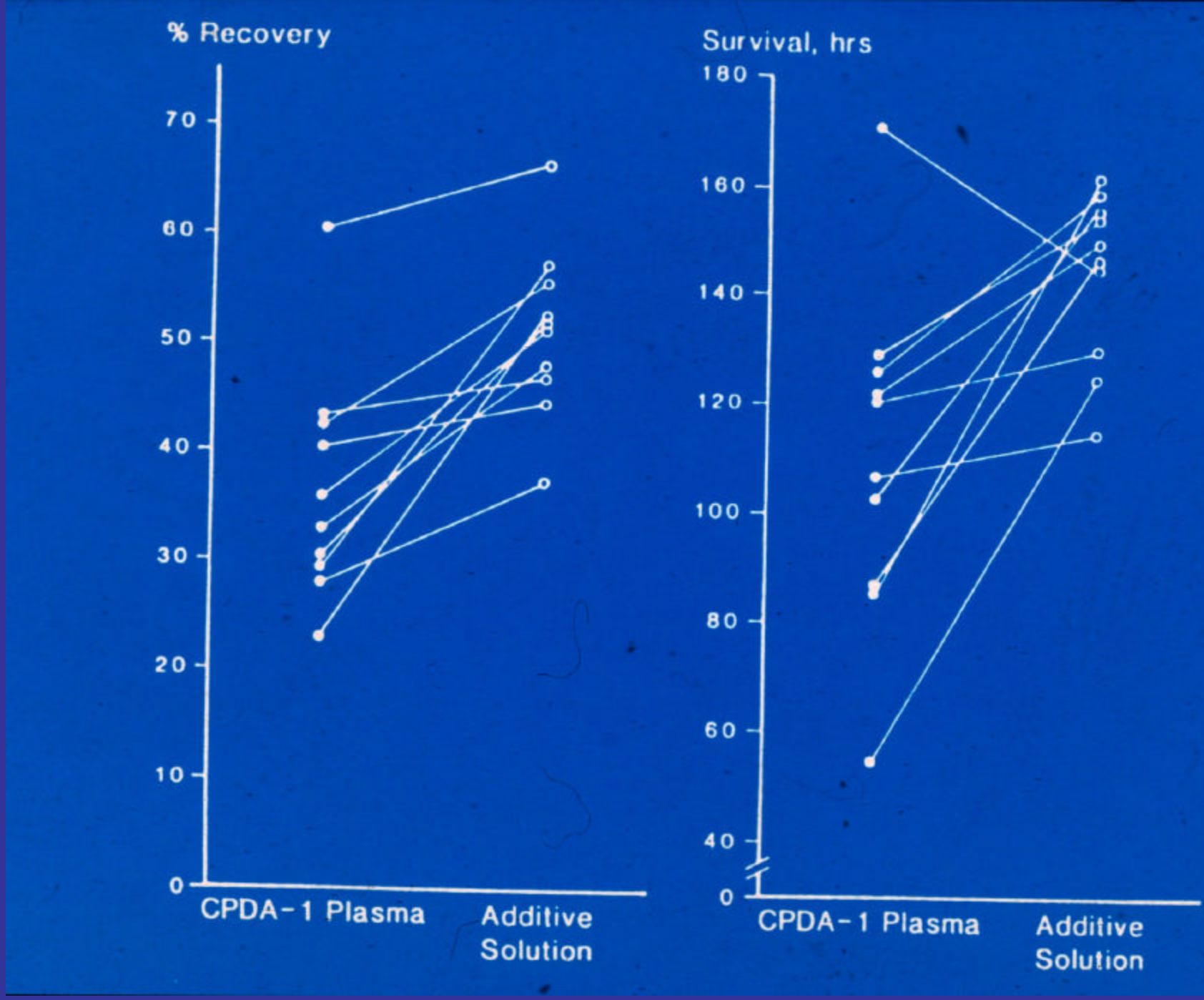
1. Variable splenic volume – 60-200 mL
2. Splenic pool varies inversely with platelet count
3. Estimation of blood volume by surface area
4. Different labs get different results

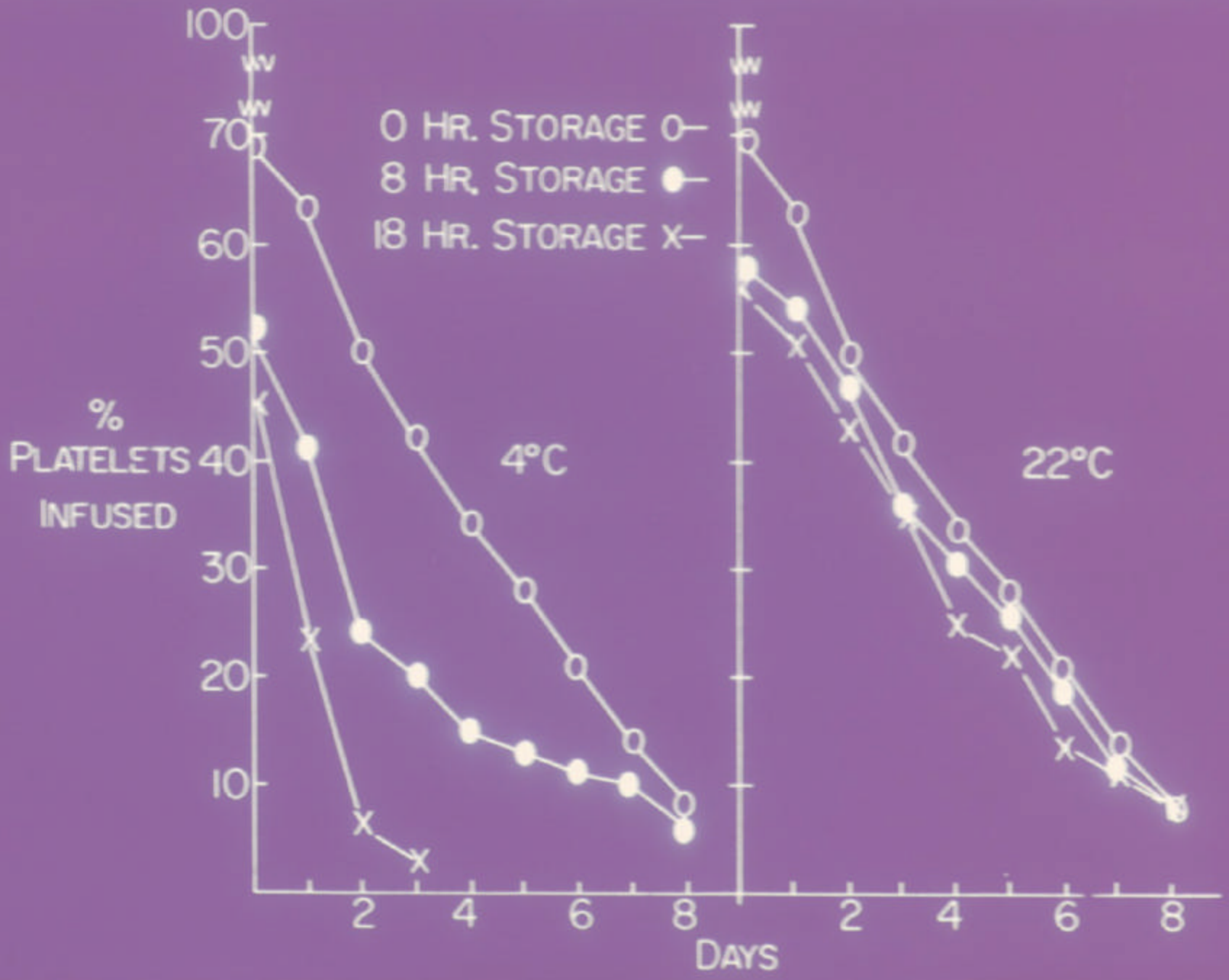

PC STORAGE, 22°c
CLX
SURVIVAL
$T_{1/2}$
6
5
4
3
2
CPD
CPD-A
— MEAN
0
1
2
3
5
7
DAYS OF STORAGE


3 DAY STORAGE - PE
○ F. WHEEL
● FLAT BED
IN VIVO RECOVERY (%)
50
40
30
20
10
0
$T_{1/2}$ (DAYS)
5
4
3
2
1
0


5 DAY PC STORAGE, 22° C
FLAT BED AGITATION
% RECOVERY
60
50
40
30
20
10
0
p=0.004
CLX
PL-146
SURV. $T_{1/2}$ (DAYS)
6
5
4
3
2
1
0
p=0.023
CLX
PL-146


70
60
50
40
30
20
10
% YIELD
7
10
DAYS
OF STORAGE


% Recovery
70
60
50
40
30
20
10
0
CPDA-1 Plasma
Additive Solution
Survival, hrs
180
160
140
120
100
80
60
40
0
CPDA-1 Plasma
Additive Solution


100
70
60
50
40
30
20
10
% PLATELETS INFUSED
0 HR. STORAGE 0—
8 HR. STORAGE ●—
18 HR. STORAGE X—
4°C
22°C
2
4
6
8
2
4
6
8
DAYS

Lotter MG et al.

A computer program in compiled BASIC for the IBM personal computer to calculate the mean platelet survival time with the multiple-hit and weighted mean methods.

Comput Biol Med 18:305, 1988

Cost Program

Program and perhaps its variations in wide use

Varying methods to calculate recovery using COST program

1. Highest value on day 0
2. Extrapolation of survival line back to day 0
3. #2, omit outliers

Current Paradigms

1. Test and control – same individual
2. Test and control – same time – two isotopes

Two Questions

What is the best control?

What do we mean by “same time”?

Paradigm - 2002

Has to be a paired control in same donor

Typical control - “ROP” - regular old platelets

- at end of licensed storage interval

- perhaps worst case scenario

Problems With Paradigm

- No “line in the sand” - ? 40% Rec., 5 day MCL
- No delineation of acceptable inferiority for test vs control, if any
- ROP will vary widely from study to study
- Creeping inferiority: $X_O \rightarrow X_1 \rightarrow X_2 \ldots X_n$

A Proposal

- Control should be fresh platelets
- Experimental results should be expressed as % of control
- Acceptable after storage:
  - Recovery: 2/3 fresh
  - Survival: 1/2 fresh
- Acceptable to have a predetermined reduction for experimental relative to extent of patient benefit

Why More Lenient Standard-MCL

In practice, time to next transfusion is no more than 2-3 days

What is the “Same Time”?

Collect and label fresh platelets:

1. On the day test is obtained
2. On the day test is reinfused

How to Prepare Fresh Control

1. Collect a unit of whole blood in plastic container and prepare a traditional platelet concentrate
2. Collect 50-100 mLs of blood in plastic tube and process to obtain platelets